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PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
FORD, ALLISON M	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/676,868	SLIVKA ET AL.	
	Examiner	Art Unit	
	ALLISON M. FORD	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8-11,15 and 17-41* is/are pending in the application.

4a) Of the above claim(s) *8-11,15 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,17,18 and 20-41* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's submission filed on 6/23/2009 has been entered. Claims 1 and 41 have been amended; claims 1, 8-11, 15 and 17-41 remain pending.

Applicants elected the species of bioabsorable materials, specifically SIS, as the repair material; cells from spinal discs as the cell type to be seeded within the repair material; bone marrow as the type of autologous medium combined with the repair material; and GDF-5 as the bioactive factor to be combined with the repair material, **with traverse** in the reply filed 4/17/2006. Per the elections claims 8-11, 15 and 19 have been withdrawn from consideration pursuant to 37 CFR 1.142(b), as being directed to non-elected species, there is currently no allowable generic claim. Claims 1, 17, 18 and 20-41 have been considered on the merits.

Response to Remarks

Applicant's remarks have been fully considered in combination with the amendments, and each will be addressed below, as appropriate. Rejections/objections not repeated herein have been withdrawn.

Claim Objections

Claim 1 is objected to for the following minor informalities: The abbreviation "SIS" should be preceded by the full term "small intestinal submucosa" the first time it is used in the claims. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The amendments to claims 1 and 41 have obviated the previous grounds of rejection under 35 USC 112, second paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

First, Applicants have traversed the rejection under 35 USC 103(a) on the grounds that Bilbo does not contemplate any folding of the ICL in order to create an annular plug. Applicants summarize the relevant portions of Bilbo, each of which report using multiple pieces of ICL to create the desired thickness, not a single piece which has been folded, and thus assert Bilbo teaches away from the instant invention which requires an active step of folding.

In response, it is initially submitted that Bilbo does teach the ICL tissue may be folded (See Bilbo, paragraph 0039), though a step of folding is not explicitly stated in Example 14 of Bilbo, it is respectfully reiterated that the rejection of record does not assert any one reference to anticipate the claimed subject matter. Rather, only when the teachings of the prior art are viewed in combination, and taken in view of the knowledge held by one having ordinary skill in the art, is the invention as currently claimed found obvious. While Example 14 of Bilbo does not teach folding or rolling the ICL material to permit introduction into the disc treatment site, it is submitted that Bilbo does suggest the ICL may be folded or rolled or otherwise physically modified as necessary; thus Bilbo cannot be considered to teach away from folding or twisting the ICL (SIS) material, because they do specifically contemplate such.

Furthermore, a separate reference has been made of record to support that folding the implant material was another art-recognized means by which a larger volume of implant material may be provided

to a defect site through a small opening: Lim et al. Lim et al is relied upon to evidence that one having ordinary skill in the art would have routinely folded, curled or rolled a graft material which is to be implanted into a defect site, prior to insertion, when the access point to the defect site is smaller than the defect site, per se (See, *e.g.* Li et al, as they disclose rolling, curling or folding (all which read on twisting) an implant material to accommodate insertion into a cavity through a small opening, at col. 4, ln 40-55). Therefore, while neither Gan et al nor Bilbo exemplify folding or twisting the implant in the treatment of intervertebral disc defects, it is maintained that the rejection of record appropriately supports the holding that a step of folding or twisting an implant material comprised of SIS in the method of Gan et al would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Second, Applicants have traversed the rejection under 35 USC 103(a) on the grounds that the Examiner has relied on impermissible hindsight. Applicants assert that, while one would have found it *prima facie* obvious to provide a ready-made implant having the size and shape of the defect, it was not *prima facie* obvious to replace the ready-made SIS implant with one which must be first molded by the surgeon. Applicants further assert there is no teaching or even suggestion to fold an SIS implant prior to insertion.

In response to Applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case each of the claim limitations has been shown to be specifically taught or suggested by the prior art, and reasoning, either

directly from the cited references, or based on knowledge generally available to the artisan in the field at the time the invention was made, has been cited to support combination of the teachings.

In response to the argument that one having ordinary skill in the art would not have found it *prima facie* obvious to replace a ready-made SIS implant with one which must be first molded by the surgeon, it is respectfully submitted that Gan et al provide specific suggestion that the implant material may treated so that it fits the specific defect site into which it is being placed (See Gan et al col. 9, ln 19-31). Furthermore, one having ordinary skill in the art would have appreciated that each intervertebral disc treatment site may differ in size and shape, based on variations in patient age, sex and size; thus, it is maintained that, based on the desire to optimize the correlation between the size/shape of the implant material and the individual defect site, provision of a material which size/shape may be manipulated would have been *prima facie* obvious. Furthermore, an implant material based on SIS, as taught by Bilbo, would be able to be manipulated on site, and thus would have been an obvious selection for substitution for the material of Gan et al. SIS is a soft-tissue, as such, it may be easily folded, rolled, cut and/or otherwise manipulated as necessary by one having ordinary skill in the art.

Third, Applicants have traversed the rejection under 35 USC 103(a) on the grounds that, even if it were somehow held obvious to manipulate the size and shape of the SIS repair material such that it corresponds in size and shape to the defect, no evidence has been provided to support that it would have been obvious to use a thin, flat sheet of the claimed dimensions as the starting material for the molding.

In response, it is respectfully submitted that the ICL (SIS) material of Bilbo, which may be substituted for the implant material of Gan et al, does have the claimed dimensions (See Bilbo, paragraph 0039). Therefore, the argument is not found persuasive.

Fourth, Applicants have traversed the rejection under 35 USC 103(a) on the grounds that, even if it were somehow obvious to modify the size and shape of the SIS repair material such that it corresponds to the size and shape of the defect site, the prior art only suggests such manipulations may be achieved by making the pieces smaller (as in Bilbo) or through use of a memory shape material (as in Li et al).

In response, it is respectfully submitted that both Gan et al and Bilbo report the shape and form of the implant material may be modified (See Gan et al, col. 9, ln 19-31 & Bilbo, paragraph 0039); the fact that each of the references instructs one to carry out such modifications is evidence that such modifications are within the technical skill of the ordinary artisan. A patent specification need not teach, and preferably omits, what is well known in the art. See *Hybritech Inc. v. Monoclonal Antibodies, Inc*, 802 F.2d 1367, 1384, 231 USPQ 31, 94 (Fed. Cir. 1986). Modifying the shape and/or form of a malleable object, such as SIS, is well within the skill level of the artisan. Therefore, the argument is not found persuasive.

Fifth, Applicants have traversed the rejection under 35 USC 103(a) on the grounds that Gan et al teaches sintered bioactive glass as their preferred embodiment, and while the Examiner has previously asserted that the reference may be relied upon for all that it teaches, not merely the preferred embodiment, Applicants request the Examiner to point to which portion of Gan et al is being relied upon.

In response, Applicants are directed to column 5, lines 12-22 (as cited), wherein Gan et al disclose the method may be carried out with a biodegradable substrate. Biodegradable substrates are not limited to sintered bioactive glass, but rather include all known biodegradable substrates. Furthermore, the rejection is not based on any of the disclosed species of biodegradable substrates of Gan et al, but rather on use of SIS, as disclosed by Bilbo, the substitution being obvious based on the fact that both materials of Gan et al and Bilbo are suitable for use in implantation into intervertebral disc defects. Therefore the argument is not found persuasive.

For simplicity the rejections have been separated out to rely only on the references relevant to the rejected claims:

Claims 1, 17, 18 and 41 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gan et al (US Patent 5,964,807), in view of Bilbo (US 2007/0250177) and Li et al (US Patent 6,764,514).

Gan et al disclose a method for repairing spinal disc defects, comprising removing damaged tissue from the nucleus pulposus (preparing a disc treatment site), preparing a hybrid material of intervertebral cells, such as nucleus pulposus cells, and a biodegradable substrate material (providing a cell-seeded defect repair material); and inserting the hybrid material into the intervertebral space to be repaired (See Gan et al, col. 5, ln 12-22).

Gan et al differs from the instant invention in that Gan et al does not disclose SIS as the biodegradable substrate material, which is used in conjunction with cells to create the cell-seeded defect repair material.

However, SIS was known as a suitable graft material for use in tissue defect repair, including for repair of intervertebral discs, see, e.g. Bilbo. Like the hybrid materials of Gan et al, the ICL grafts of Bilbo can be seeded with cells and/or bioactive factors, including growth factors (See Bilbo, paragraph 0052). ICL is derived from porcine SIS. The ICL graft material of Bilbo is manufactured in the form of a flat sheet, having a thickness of only 0.20-0.25 mm and a planar size of 5.0 x 5.0 cm (50 x 50 mm) to 12 x 36 cm (120 x 360 mm) (See Bilbo, paragraph 0039) (which read on the dimensions as claimed). Bilbo discloses the ICL sheet may be subjected to physical modifications, such as shaping, prior to use (See Bilbo paragraph 0017), including rolling or folding for tissue bulking or augmentation applications (See Bilbo paragraph 0043). Bilbo disclose bioengineered grafts comprised of ICL for implantation into intervertebral disc defect sites (See Bilbo, Pg. 14, paragraphs 0120-0124).

It has been held that substitution of a known element for another to yield predictable results would have been obvious to one of ordinary skill in the art. In the instant case, both Gan et al and Bilbo report methods for repairing damaged intervertebral discs, by removing the damage disc, and inserting a defect repair material into the defect site, each of the repair materials yield the same result: occlusion of the defect site, permitting regeneration of natural tissue. Thus, substitution of the ICL (SIS material) (as disclosed by Bilbo) for the substrate material of the hybrid material in Gan et al, would have been obvious to one of ordinary skill in the art.

With regards to the shape of the hybrid material (defect repair material), Gan et al state the hybrid treatment material may be shaped as necessary for insertion into the defect (See Gan et al col. 9, ln 19-31). One of ordinary skill in the art would have found it *prima facie* obvious to optimize the shape of the repair material so as to correlate as closely as possible with the defect site to be repaired, or such that the repair material will correlate as closely as possible with the defect site to be repaired upon implantation. Such reasoning would also hold true when substituting the ICL (SIS) of Bilbo in the method of Gan et al, as well. One would have had a reasonable expectation of manipulating the shape of the ICL (SIS) repair material of Bilbo based on the fact that Bilbo disclose the planar ICL (SIS) material can be physically modified as deemed necessary for downstream applications (See Bilbo, paragraph 0043). It has been held that differences in the shape of a material, when the shape would be routinely optimized based on the recognized use/need, are considered to be obvious. See *In re Dailey, 357 F.2d 669, 149 USPQ 47 (CCPA 1966)*. For the same reasons, it is further submitted that manipulation of the repair material of Bilbo into the form of a mushroom shape, if the defect site to be repaired has a mushroom shape, would be *prima facie* obvious.

Gan et al further differs from the instant invention in that while they disclose implanting the repair material into the disc defect, they do not specifically state the repair material is folded, twisted or otherwise manipulated as part of the insertion step. However, it is submitted that one of ordinary skill in the art will recognize that folding, twisting or otherwise manipulating the repair material may be necessary in order to successfully insert the material into the defect site (See, *e.g.* Li et al, as they disclose rolling, curling or folding (all which read on twisting) an implant material to accommodate insertion into a cavity through a small opening, at col. 4, ln 40-55). Clearly if the opening made to the intervertebral disc space is smaller than the actual repair material, it would be necessary to fold, or twist the repair material in order to manipulate it through the opening into the defect site. In such cases the repair material may be of a form wherein the material will correlate in size and shape with the defect only after implantation (i.e. such as in a strip form, wherein the strip is folded, twisted or rolled so as to fill a voluminous cavity).

This rationale holds true for any implant material, including the ICL (SIS) taught by Bilbo (as discussed above). One would have had a reasonable expectation that the cell-seeded SIS materials could be manipulated, twisted or folded as necessary based on the fact that SIS is, due to its structure, flexible and malleable and because Bilbo specifically states the material can be folded and/or rolled (See Bilbo, paragraph 0043). Therefore, folding of the implant material prior to insertion to the defect site, in order to aide in insertion, would have been recognized as *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Claims 1, 17, 18, 23-31 and 41 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gan et al (US Patent 5,964,807), in view of Bilbo (US 2007/0250177), Li et al (US Patent 6,764,514), and Lim et al (WO 03/51239).

The teachings of Gan et al, Bilbo, and Li et al have been set forth above. The combination has been held to render obvious the subject matter of claims 1, 17, 18 and 41.

Gan et al differs from some aspects of the instant invention in that, while they disclose including bioactive factors, including transforming growth factor-beta, in the biodegradable implant material (See col. 8, ln 62-col. 9, ln 5), they do not specify the growth factor GDF-5. It is noted that Gan et al teach growth factors, including transforming growth factor-beta enhances cell growth (See Gan et al, col. 8, ln 62-66). A person of ordinary skill, in reading Gan et al, would have recognized the desirability of improving cell growth within the hybrid material. This rationale is extendable to any implant material used in the method of Gan, including the ICL (SIS) taught by Bilbo (as discussed above).

Lim et al teaches that GDF-5 is one of a finite number of growth factors included in the transforming growth factor-beta family, known to be useful for promoting cartilage growth (chondroinductive properties) (See Lim et al, Pg. 7, ln 9-23). Thus, it would have been obvious to a person of ordinary skill in the art to try GDF-5 as the particular transforming growth factor-beta protein provided to the implant material in an attempt to provide improved cell growth within the implant material upon implantation. It has been held that "a person with ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense." See *KSR International Co. v Teleflex, Inc.* 82 USPQ2d 1385 at 1390. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 17, 18, 20-22 and 41 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gan et al (US Patent 5,964,807), in view of Bilbo (US 2007/0250177), Li et al (US Patent 6,764,514), and Moehlenbruck et al (US Patent 6,723,335).

The teachings of Gan et al, Bilbo, and Li et al have been set forth above. The combination has been held to render obvious the subject matter of claims 1, 17, 18 and 41.

Gan et al differs from some aspects of the instant invention in that they do not disclose combining the repair material with autologous bone marrow prior to insertion into the defect site. However, at the time the invention was made, it was known in the art to be beneficial to include autologous bone marrow in intervertebral disc implant materials to increase regeneration *in situ* (See, e.g. Moehlenbruck et al, col. 5, ln 6-30); thus one of ordinary skill would have been motivated to further apply autologous bone marrow to the implant material of Gan et al, for the predictable result of increasing regeneration of the disc tissue *in situ*. This rationale is extendable to any implant material used in the method of Gan et al, including the ICL (SIS) taught by Bilbo (as discussed above). One would have had a reasonable expectation of successfully providing and applying bone marrow to the implant material because Moehlenbruck et al disclose that use of bone marrow in intervertebral disc implants was within the purview of the artisan of ordinary skill (See Moehlenbruck et al, col. 5, ln 6-30).

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 17, 18 and 20-41 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gan et al (US Patent 5,964,807), in view of Bilbo (US 2007/0250177), Li et al (US Patent 6,764,514), Lim et al (WO 03/51239), and Moehlenbruck et al (US Patent 6,723,335).

The teachings of Gan et al, Bilbo, and Li et al have been set forth above. The combination has been held to render obvious the subject matter of claims 1, 17, 18 and 41.

The teachings of each of Lim et al and Moehlenbruck et al have also been set forth above, and have been shown to be individually combinable with the method rendered obvious by Gan et al, Bilbo and Li et al to render obvious the subject matter of claims 20-31.

Yet it is further submitted that it would have been *prima facie* obvious to one having ordinary skill in the art, at the time the invention was made to include both the GDF-5 growth factor, suggested by Lim et al, and bone marrow, as suggested by Moehlenbruck et al, in the implant material used in the method suggested by Gan et al, Bilbo and Li et al. The rationale for holding the combination obvious is based on the rationale that combining multiple elements, each taught in the prior art, to yield a combination with predictable results (e.g. the combined effect of each individual element) is *prima facie* obvious. See *KSR International Co. v Teleflex Inc* 82 USPQ2d 1385 (U.S. 2007). In the instant case each of GDF-5 and bone marrow are recognized agents which would be expected to improve the efficacy of the implant material, therefore provision of both agents together would be expected to yield an additive effect. Therefore, the invention as a whole would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALLISON M. FORD whose telephone number is (571)272-2936. The examiner can normally be reached on 8:00-6 M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Allison M. Ford/
Primary Examiner, Art Unit 1651